

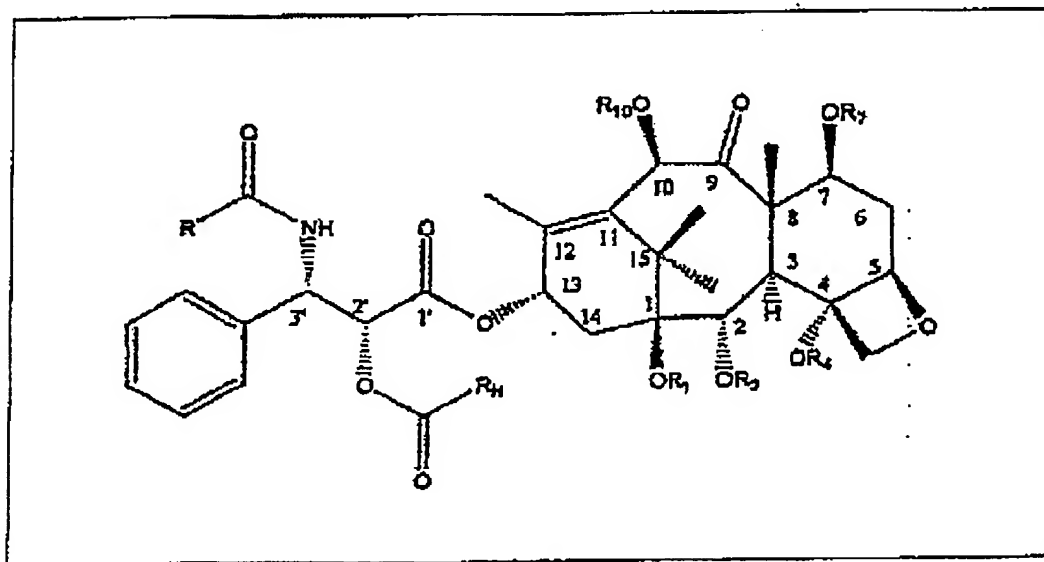
Appl. No.: 10/510,120

Amdt. dated 05/08/2006

Reply to Office action of December 6, 2005

Amendments to the Claims:

1. (Currently Amended) A method of converting a taxane molecule having the formula:



wherein

R₁ is hydrogen, an alkyl group, an aryl group, an ester group, an ether group, or a hydroxyl protecting group;

R₂ is hydrogen, an alkyl group, an aryl group, an ester group, an ether group, or a hydroxyl protecting group;

R₄ is hydrogen, an alkyl group, an aryl group, an ester group, an ether group, or a hydroxyl protecting group;

R₇ is hydrogen, an alkyl group, an aryl group, an ester group, an ether group, a glycoside group, an oxo-group, or a hydroxyl protecting group;

R₁₀ is hydrogen, an alkyl group, an aryl group, an ester group, an ether group, or a hydroxyl protecting group;

R is an alkoxy group, an alkyl group, an aryl group, an arylalkyl group, an ether group, heterocyclic group, or a vinyl group; and

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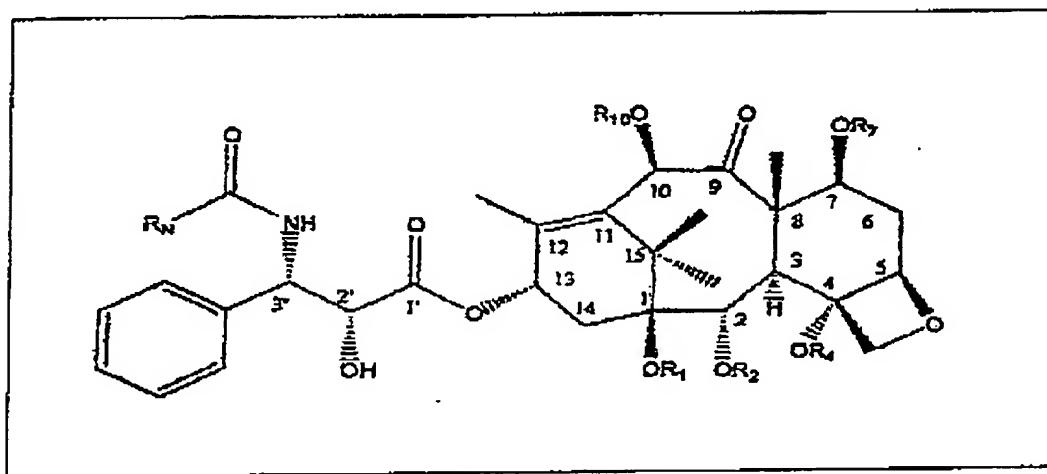
R_N is an alkoxy group, an alkyl group, an aryl group, an arylalkyl group, an ether group, or a heterocyclic group, or a vinyl group;

the method comprising the steps of:

reductively deoxygenating the C-3' amide group on the taxane molecule to form an a C-3' imine compound;

hydrolyzing the imine compound to form a primary amine compound; and

treating the primary amine compound with a hindered base to form another taxane molecule having the formula:



wherein

R_1 , R_2 , R_4 , R_7 , R_{10} , and R_N are as defined above.

2. (Currently Amended) The method of claim 1 wherein the step of reductively deoxygenating the C-3' amide group on the taxane compound comprises ~~conducting~~ contacting the taxane compound with a transition metal reducing agent.

3. (Original) The method of claim 2, wherein the transition metal reducing agent is Schwartz's reagent (zirconocene chloride hydride).

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4. (Original) The method of claim 2, wherein the transition metal reducing agent is an analogue or derivative of Schwartz's reagent.

5. (Original) The method of claim 2, wherein the transition metal reducing agent is selected from the group consisting of titanium-containing reducing agents, hafnium-containing reducing agents, niobium-containing reducing agents, and molybdenum-containing reducing agents.

6. (Original) The method of claim 1 wherein the step of hydrolyzing the imine compound comprises contacting the imine compound with an acid.

7. (Original) The method of claim 6 wherein the acid is sulfuric acid.

8. (Original) The method of claim 1 wherein the step of treating the primary amine compound with a base comprises treating the primary amine compound with triethylamine.

9. (Original) The method of claim 1 wherein the step of treating the primary amine compound with a base comprises treating the primary amine compound with triethylamine and anthranilic acid.

10. (Original) The method of claim 1, further comprises the step of chelating the transition metal reducing agent or by-products thereof by adding a chelating agent.

11. (Original) The method of claim 1, wherein the chelating step comprises chelating the transition metal reducing agent or by-products thereof with a zirconium chelator.

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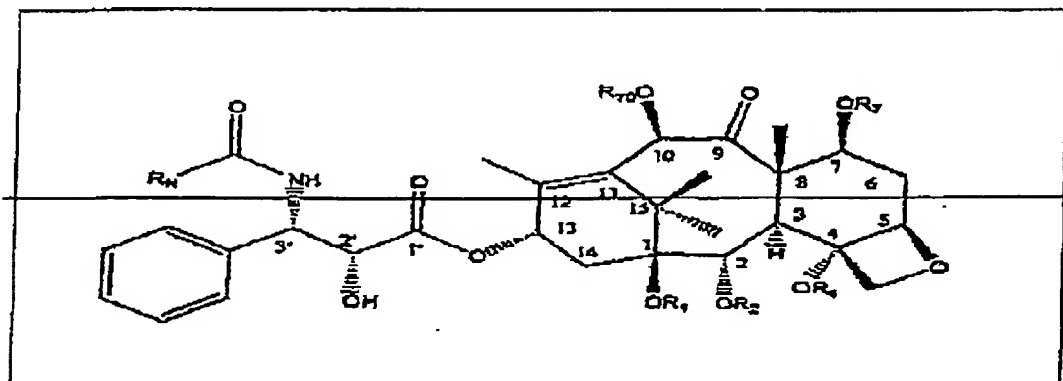
12. (Original) The method of claim 11, wherein the chelating step comprises chelating the transition metal reducing agent or by-products thereof with N, N-bis (2-hydroxyethyl) glycine (bicine).

13. (Currently Amended) The method of claim 11, wherein the chelating step comprises chelating the transition metal reducing agent or by-products thereof with an agent comprising a chelating agent selected from the group consisting of ethylene diamine tetra acetic acid (EDTA), ethylene glycol (bis) aminoethyl ether tetra acetic acid (EGTA), 1,2-bis- (o-aminophenoxy) ethane-N, N, N', N'[[L]] -tetra-acetic acid (BAPTA), N, N, N', N'-tetrakis- (2-pyridylmethyl) ethylenediamine (~~TPEN~~) (TPEN), nitrilotriacetic acid, TIRON® and analogues and derivatives thereof.

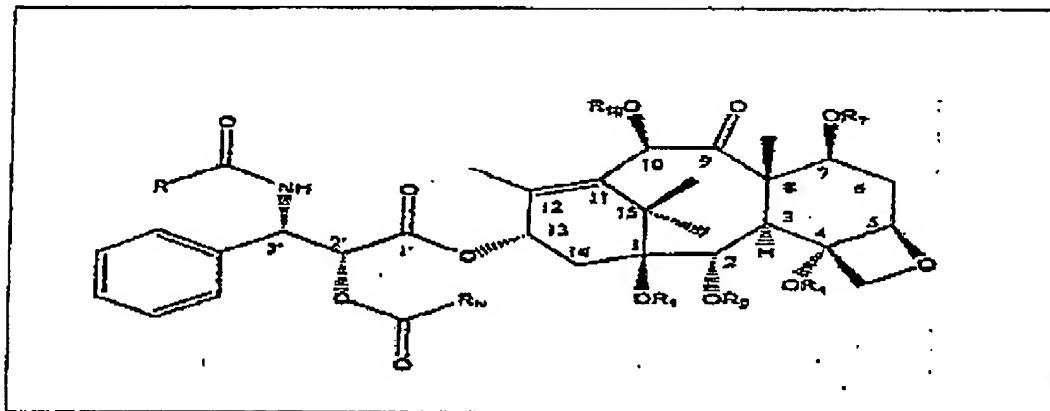
14. (Original) The method of claim 1 wherein the imine compound and the primary amine compound are not isolated prior to the next step.

15. (Original) The method of claim 1 wherein R_N is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, tert-butoxy.

16. (Currently Amended) A method of converting a taxane molecule having the formula:



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wherein

R₁ is hydrogen;

R₂ is a benzoyl group;

R₄ is an acetate group;

R₇ is hydrogen;

R₁₀ is hydrogen or an acetate group;

R is an alkoxy group, an alkyl group, an aryl group, an arylalkyl group, an ether group, heterocyclic group, or a vinyl group; and

R_N is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, or tert-butoxy ;

the method comprising the steps of :

reacting the taxane molecule with zirconocene chloride hydride in a solvent to form an imine compound;

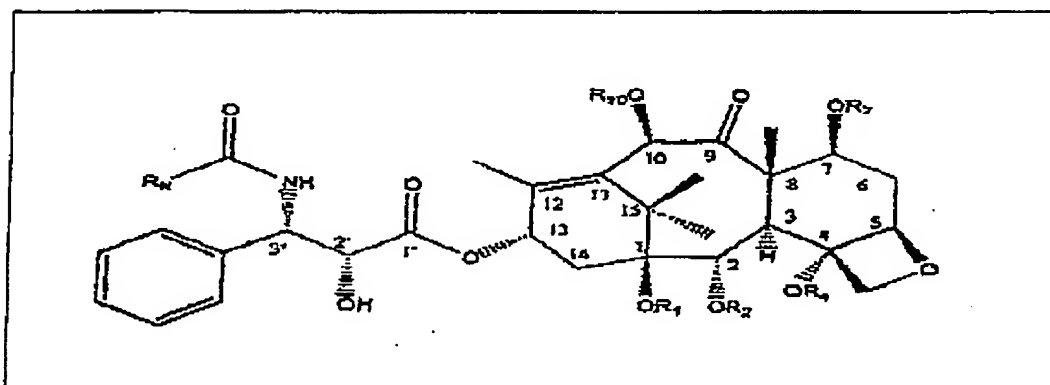
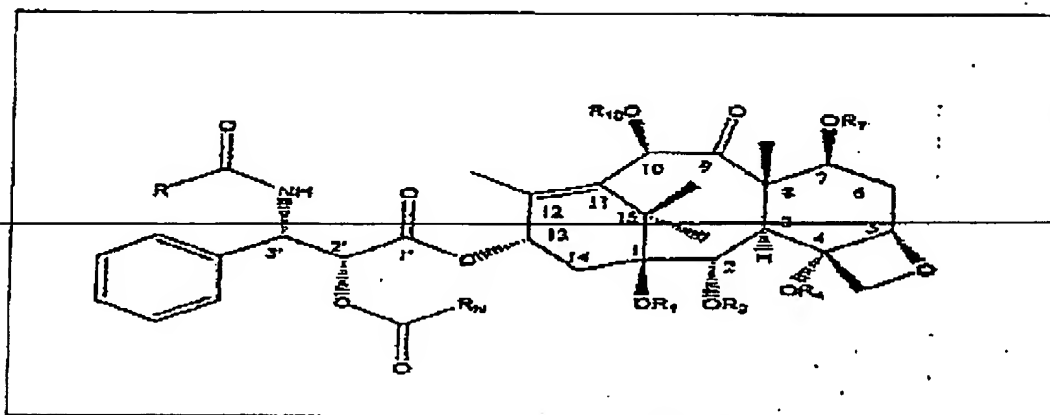
hydrolyzing the imine compound to form a primary amine compound; and

treating the primary amine compound with a base to form another taxane molecule having the formula:

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wherein

R₁, R₂, R₄, R₇, R₁₀, and R_N are as defined above.

17. (Original) The method of claim 16 wherein the step of reacting the taxane molecule comprises reacting the taxane molecule with about 3 or more molar equivalents of zirconocene chloride hydride.

18. (Original) The method of claim 17 wherein reacting the taxane molecule with zirconocene chloride hydride comprises reacting the taxane molecule with zirconocene chloride hydride at a temperature below about 15° C.

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19. (Original) The method of claim 16 wherein the solvent is tetrahydrofuran.
20. (Original) The method of claim 16 wherein the step of hydrolyzing the imine compound comprises treating the imine compound with an acid.
21. (Currently Amended) The method of claim 20, wherein the step of hydrolyzing the imine compound comprises treating the ~~amine~~ imine compound with sulfuric acid.
22. (Original) The method of claim 16, wherein the step of treating the primary amine compound with a base comprises treating the primary amine compound with triethylamine.
23. (Original) The method of claim 16, wherein the step of treating the primary amine compound with base comprises treating the primary amine compound with triethylamine and anthranilic acid.
24. (Original) The method of claim 16 comprising the step of chelating the zirconocene chloride hydride and other zirconium by-products prior to hydrolyzing the imine compound with a chelating agent.
25. (Original) The method of claim 16, wherein the chelating step comprises chelating the transition metal reducing agent or by-products thereof with N, N-bis (2-hydroxyethyl) glycine (bicine).
26. (Currently Amended) The method of claim 16, wherein the chelating step comprises chelating the transition metal reducing agent or by-products thereof with an agent comprising a chelating agent selected from the group consisting of ethylene diamine tetra acetic acid (EDTA), ethylene glycol (bis) aminoethyl ether tetra acetic acid (EGTA), 1,2-bis- (o-aminophenoxy)ethane-N, N, N', N'[[,]] -tetra-acetic ~~acetic~~ acetic acid (BAPTA), N, N, N', N'-tetrakis-

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(2-pyridylmethyl) ethylenediamine (~~TPEN~~) (TPEN), nitrilotriacetic acid, TIRON® and analogues and derivatives thereof.

27. (Original) The method of claim 16 wherein R_{10} is hydrogen.
28. (Original) The method of claim 27 wherein R_N is phenyl, and R is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, or *tert*-butoxy.
29. (Original) The method of claim 27 wherein R_N is 1-methyl-1-propenyl, and R is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, or *tert*-butoxy.
30. (Original) The method of claim 27 wherein R_N is n-pentyl, and R is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, or *tert*-butoxy.
31. (Original) The method of claim 16 wherein R_{10} is an acetate group.
32. (Original) The method of claim 31 wherein R_N is phenyl, and R is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, or *tert*-butoxy.
33. (Original) The method of claim 31 wherein R_N is 1-methyl-1-propenyl, and R is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, or *tert*-butoxy.
34. (Original) The method of claim 31 wherein R_N is n-pentyl, and R is phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, or *tert*-butoxy.

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35. (Original) The method of claim 35, further comprises the step of dictating the zirconocene chloride hydride and other zirconium by-products thereof by adding a chelating agent.

36. (Original) The method of claim 35, wherein the chelating step comprises adding zirconium chelator.

37. (Original) The method of claim 35, wherein the chelating step comprises chelating the transition metal reducing agent or by-products thereof with N, N-bis (2-hydroxyethyl) glycine (bicine).

38. (Currently Amended) The method of claim 35, wherein the chelating step comprises adding a ~~chelating~~ chelating agent comprising a chelating agent selected from the group consisting of ethylene diamine tetra acetic acid (EDTA), ethylene glycol (bis) ~~aminoethyl~~ aminoethyl ether tetra acetic acid (EDTA) (EGTA), 1, 2-bis- (O-aminophenoxy) ethane-N, N, N',N'[[,]]-tetra-acetic acid (BAPTA), N, N, N', N'-tetrakis- (2-pyridylmethyl) ethylenediamine ~~(TIPEN)~~ (TPEN), nitrilotriacetic acid, TIRON® or analogues thereof.

39. (Original) The method of claims 1 or 16, further comprising the step of removing substantially all of the transition metal or transition metal by-products by complexation, precipitation, filtration, centrifugation, electrochemical methodology, chromatography, chelation or any combination thereof.

40. (Currently Amended) A method of converting an acyl-protected taxane molecule, the method comprising the steps of:

reductively deoxygenating an amide group on the taxane molecule to form an imine compound;

hydrolyzing the imine compound to form a primary amine compound; and

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treating the primary amine compound with a hindered base to effect acyl migration and
form another taxane molecule.

41. (Currently Amended) The method of claim 40, wherein the step of reductively
deoxygenating an amide group on the taxane compound comprises conducting the taxane
compound with a transition metal reducing agent.

42. (Original) The method of claim 40, wherein the step of hydrolyzing the imine
compound comprises contacting the imine compound with an acid.

43. (Original) The method of claim 40, wherein the step of treating the primary
amine compound with a base comprises treating the primary amine compound with
triethylamine.